Amendments to the Claims:

The Listing of Claims will replace all prior versions and listings of claims in the specification:

Listing of Claims:

1. (original) A crystal comprising an angiotensin-converting enzyme-related carboxypeptidase or homologue thereof.

2. (original) The crystal according to claim 1, further comprising a chemical entity, wherein said chemical entity binds to the angiotensin-converting enzyme-related carboxypeptidase or homologue thereof.

3. (original) The crystal according to claim 2, wherein the chemical entity binds to the active site on angiotensin-converting enzyme-related carboxypeptidase or homologue thereof.

4. (original) The crystal according to claim 3, wherein the chemical entity is selected from the group consisting of (S,S)2-{1-Carboxy-2-[3-(3,5-dichloro-benzyl)-3*H*-imidazol-4-yl]-ethylamino}-4-methyl-pentanoic acid, (S,S)2-{1-Carboxy-2-[3-(4-iodo-benzyl)-3*H*-imidazol-4-yl}-ethylamino}-4-methyl-pentanoic acid, (S,S)2-[2-(6-Bromo-benzothiazol-2-ylcarbamoyl)-1-carboxy-ethylamino]-4-methyl-pentanoic acid and (S, S)2-{1-Carboxy-2-[3-(3,5-dichloro-benzyl)-3*H*-imidazol-4-yl]-ethylamino}-4-phenyl-butyric acid.

5. (original) The crystal according to claim 3, wherein the chemical entity is (S,S)2-{1-Carboxy-2-[3-(3,5-

dichloro-benzyl)-3*H*-imidazol-4-yl]-ethylamino}-4-methyl-pentanoic acid.

6. (currently amended) The crystal according to claim 1 or 2, wherein said angiotensin-converting enzyme-related carboxypeptidase is selected from the group consisting of amino acid residues 1-740 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~, amino acid residues 19-740 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~, amino acid residues 1-611 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~ and amino acid residues 19-611 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~.

7. (currently amended) The crystal according to claim 1 or 2, wherein said angiotensin-converting enzyme-related carboxypeptidase comprises amino acid residues 19-740 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~.

8. (original) An isolated, substantially pure, angiotensin-converting enzyme-related carboxypeptidase protein.

9. (original) A crystallizable composition comprising an angiotensin-converting enzyme-related carboxypeptidase or homologue thereof.

10. (original) The crystallizable composition according to claim 9, further comprising a chemical entity.

11. (original) The crystallizable composition according to claim 10, wherein the chemical entity binds to the

active site on angiotensin-converting enzyme-related carboxypeptidase or homologue thereof.

12. (original) The crystallizable composition according to claim 11, wherein the chemical entity is selected from the group consisting of (S,S)2-{1-Carboxy-2-[3-(3,5-dichloro-benzyl)-3*H*-imidazol-4-yl]-ethylamino}-4-methyl-pentanoic acid, (S,S)2-{1-Carboxy-2-[3-(4-iodo-benzyl)-3*H*-imidazol-4-yl}-ethylamino}-4-methyl-pentanoic acid, (S,S)2-[2-(6-Bromo-benzothiazol-2-ylcarbamoyl)-1-carboxy-ethylamino]-4-methyl-pentanoic acid and (S, S)2-{1-Carboxy-2-[3-(3,5-dichloro-benzyl)-3*H*-imidazol-4-yl]-ethylamino}-4-phenyl-butyric acid.

13. (original) The crystallizable composition according to claim 11, wherein the chemical entity is (S,S)2-{1-Carboxy-2-[3-(3,5-dichloro-benzyl)-3*H*-imidazol-4-yl]-ethylamino}-4-methyl-pentanoic acid.

14. (currently amended) The crystallizable composition according to claim 9 or 10, wherein said angiotensin-converting enzyme-related carboxypeptidase is selected from the group consisting of amino acid residues 1-740 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~, amino acid residues 19-740 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~, amino acid residues 1-611 human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~ and amino acid residues 19-611 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~.

15. (currently amended) The crystallizable composition according to claim 9 or 10, wherein said angiotensin-converting enzyme-related carboxypeptidase comprises amino acid residues 19-740 of human full-length angiotensin-converting enzyme-related carboxypeptidase ~~SEQ ID NO: 4~~.

16. (currently amended) A computer comprising:

(a) a machine-readable data storage medium, comprising a data storage material encoded with machine-readable data, wherein said data defines all or part of a binding pocket or protein selected from the group consisting of:

(i) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, P346, T371, Y510 and F512 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(ii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H364, E375, H378, E402, F504, H505, Y510, F512 and Y515 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said

angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(iii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H374, E375, H378, E398, E402, R481, L503, F504, H505, Y510, S511, F512, R514, Y515 and E564 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å; and

(iv) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues according to Figure 1A, 2A, 3A or 3B, wherein the root mean square deviation between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not more than 1.7 Å;

(b) a working memory for storing instructions for processing said machine-readable data;

(c) a central processing unit coupled to said working memory and to said machine-readable data storage medium for processing said machine-readable data and means for generating three-dimensional structural information of said binding pocket or protein; and

(d) output hardware coupled to said central processing unit for outputting three-dimensional structural information of said binding pocket or protein, or information produced using said three-dimensional structural information of said binding pocket or protein.

17. (currently amended) The computer according to claim 16, wherein the binding pocket is produced by homology modeling of the structure coordinates of said angiotensin-converting enzyme-related carboxypeptidase amino acid residues according to ~~Figures 1A, 2A, 3A or 3B~~ Figure 1A, 2A, 3A or 3B.

18. (original) The computer according to claim 16, wherein said means for generating three-dimensional structural information is provided by means for generating a three-dimensional graphical representation of said binding pocket or protein.

19. (original) The computer according to claim 16, wherein said output hardware is a display terminal, a printer, CD or DVD recorder, ZIP™ or JAZ™ drive, a disk drive, or other machine-readable data storage device.

20. (currently amended) A method for designing, selecting and/or optimizing a chemical entity that binds to all or part of a binding pocket or protein selected from the group consisting of:

(i) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, P346, T371, Y510 and F512 according to Figure 3A or 3B ~~Figures~~

~~3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(ii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H364, E375, H378, E402, F504, H505, Y510, F512 and Y515 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(iii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H374, E375, H378, E398, E402, R481, L503, F504, H505, Y510, S511, F512, R514, Y515 and E564 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å; and

(iv) a set of amino acid residues which correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues according to Figure 1A, 2A, 3A or 3B, wherein the root mean square deviation between said amino acid residues and said human angiotensin-converting

enzyme-related carboxypeptidase amino acid residues is not more than 1.7 Å;

comprising the steps of:

(a) providing the structure coordinates of all or part of said binding pocket or protein on a computer comprising the means for generating three-dimensional structural information from said structure coordinates; and

(b) designing, selecting and/or optimizing said chemical entity by performing a fitting operation between said chemical entity and said three-dimensional structural information of all or part of said binding pocket or protein.

21. (currently amended) A method of using a computer for evaluating the ability of a chemical entity to associate with all or part of a binding pocket or protein selected from the group consisting of:

(i) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, P346, T371, Y510 and F512 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(ii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H364, E375, H378, E402, F504,

H505, Y510, F512 and Y515 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(iii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H374, E375, H378, E398, E402, R481, L503, F504, H505, Y510, S511, F512, R514, Y515 and E564 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å; and

(iv) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues according to Figure 1A, 2A, 3A or 3B, wherein the root mean square deviation between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not more than 1.7 Å;

said method comprising the steps of:

(a) providing the structure coordinates of all or part of said binding pocket or protein on a computer comprising the means for generating three-dimensional structural information from said structure coordinates;

(b) employing computational means to perform a fitting operation between a first chemical entity and all or part of the binding pocket or protein; and

(c) analyzing the results of said fitting operation to quantitate the association between the chemical entity and all or part of the binding pocket or protein.

22. (original) The method according to claim 21, further comprising generating a three-dimensional graphical representation of all or part of the binding pocket or protein prior to step (b).

23. (original) The method according to claim 21, further comprising the steps of:

(d) repeating steps (b) through (c) with a second chemical entity; and

(e) selecting at least one of said first or second chemical entity that associates with said all or part of said binding pocket or protein based on said quantitated association of said first or second chemical entity.

24. (currently amended) A method for identifying an agonist or antagonist of a molecule or molecular complex comprising all or part of a binding pocket or protein selected from the group consisting of:

(i) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, P346, T371, Y510 and F512 according to Figure 3A or 3B ~~Figures~~

~~3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(ii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H364, E375, H378, E402, F504, H505, Y510, F512 and Y515 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(iii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H374, E375, H378, E398, E402, R481, L503, F504, H505, Y510, S511, F512, R514, Y515 and E564 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å; and

(iv) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues according to Figure 1A, 2A, 3A or 3B, wherein the root mean square deviation between said amino acid residues and said angiotensin-converting

enzyme-related carboxypeptidase amino acid residues is not more than 1.7 Å;

comprising the steps of:

(a) using a three-dimensional structure of all or part of the binding pocket or protein of the molecule or molecular complex to design or select a chemical entity;

(b) contacting the chemical entity with the molecule or the molecular complex;

(c) monitoring the catalytic activity of the molecule or molecular complex; and

(d) classifying the chemical entity as an agonist or antagonist based on the effect of the chemical entity on the catalytic activity of the molecule or molecular complex.

25. (currently amended) A method of designing a compound or complex that associates with all or part of a binding pocket selected from the group consisting of:

(i) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, P346, T371, Y510 and F512 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

(ii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related

carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H364, E375, H378, E402, F504, H505, Y510, F512 and Y515 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å; and

(iii) a set of amino acid residues that correspond to human angiotensin-converting enzyme-related carboxypeptidase amino acid residues N149, D269, R273, F274, H345, P346, A348, D367, T371, H374, E375, H378, E398, E402, R481, L503, F504, H505, Y510, S511, F512, R514, Y515 and E564 according to Figure 3A or 3B ~~Figures 3A or 3B~~, wherein the root mean square deviation of the backbone atoms between said amino acid residues and said angiotensin-converting enzyme-related carboxypeptidase amino acid residues is not greater than about 3.0 Å;

comprising the steps of:

(a) providing the structure coordinates of all or part of said binding pocket on a computer comprising the means for generating three-dimensional structural information from said structure coordinates; and

(b) using the computer to perform a fitting operation to associate a first chemical entity with all or part of the binding pocket;

(c) performing a fitting operation to associate at least a second chemical entity with all or part of the binding pocket;

(d) quantifying the association between the first or second chemical entity and all or part of the binding pocket;

(e) optionally repeating steps (b) to (d) with another first and second chemical entity, selecting a first and a second chemical entity based on said quantified association of all of said first and second chemical entity;

(f) optionally, visually inspecting the relationship of the first and second chemical entity to each other in relation to the binding pocket on a computer screen using the three-dimensional graphical representation of the binding pocket and said first and second chemical entity; and

(g) assembling the first and second chemical entity into a compound or complex that associates with all or part of said binding pocket by model building.

26. (currently amended) A method of utilizing molecular replacement to obtain structural information about a molecule or a molecular complex of unknown structure, comprising the steps of:

(a) crystallizing said molecule or molecular complex;

(b) generating an X-ray diffraction pattern from said crystallized molecule or molecular complex; and

(c) applying at least a portion of the structure coordinates set forth in ~~Figures 1A, 2A, 3A or 3B~~ Figure 1A, 2A, 3A or 3B or homology model thereof to the X-ray diffraction pattern to generate a three-dimensional electron

density map of at least a portion of the molecule or molecular complex whose structure is unknown.

27. (original) The method according to claim 26, wherein the molecule is an angiotensin-converting enzyme-related carboxypeptidase homologue.

28. (original) The method according to claim 26, wherein the molecular complex is selected from the group consisting of an angiotensin-converting enzyme-related carboxypeptidase protein complex and an angiotensin-converting enzyme-related carboxypeptidase homologue complex.